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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,809	10/11/2005	Pawan Seth	314840US76PCT	8871

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EXAMINER	
DICKINSON, PAUL W	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
01/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/517,809	SETH ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 5-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4 and 11-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group A in the reply filed on 10/28/2009 is acknowledged.

The traversal is on the ground(s) that for restriction to be proper the groups must be patentably distinct and there must be a serious search burden.

This is not found persuasive because search burden is not a criterion used to establish the propriety of restriction in applications filed under 35 U.S.C. 371. The standard is unity of invention. The instant claims lacks unity of invention for the reasons set forth in the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 1 encompasses all tramadol formulations that induce a statistically significant lower mean fluctuation index in the plasma than an immediate release composition comprising the same form of tramadol while maintaining bioavailability

substantially equivalent to that of the immediate release composition. This constitutes a large genus of tramadol formulations encompassing a myriad of compositions. The genus claimed encompasses any pharmaceutical forms (i.e. tablet, capsule, liquid, implant, inhalant, transdermal patch, suppository, etc) with any components, including any excipients in any amount/structure and any further active agents in any amount/structure. By contrast, the application describes only formulations comprising (i) a core comprising at least one form of tramadol selected from the group consisting of tramadol, enantiomers thereof, pharmaceutically acceptable salts thereof and combinations thereof and at least one pharmaceutically acceptable excipient; and (ii) a coating comprising at least one water-insoluble, water-permeable film-forming polymer, at least one plasticizer and at least one water-soluble polymer. This composition fails to represent all tramadol formulations having any form with any components that induces a statistically significant lower mean fluctuation index in the plasma than an immediate release composition comprising the same form of tramadol while maintaining bioavailability substantially equivalent to that of the immediate release composition. As there are insufficient representative examples to support the genus of tramadol formulations claimed, the skilled practitioner would not accept that Applicant was in possession of the claimed invention at the time of filing.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by US 6159501 ('501; document already in record). '501 discloses a modified release pharmaceutical composition comprising an opioid wherein the composition, when orally administered to a patient, induces a statistically significant lower mean fluctuation index in the plasma than an immediate release composition comprising the same opioid while maintaining bioavailability substantially equivalent to that of the immediate release composition (see abstract; col 3, line 16 to col 4, line 6; col 52, lines 33-48). Tramadol is a preferred opioid (see claim 81).

Claims 11, 17, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6156342 ('342). '342 discloses a controlled release (modified release) pharmaceutical composition comprising (i) a core comprising tramadol hydrochloride (at least one form of tramadol selected from the group consisting of tramadol, enantiomers thereof, pharmaceutically acceptable salts thereof), at least one lubricant, at least one binder, and at least one glidant; and (ii) a coating comprising cellulose acetate (a water-insoluble, water-permeable film-forming polymer), at least one plasticizer, and polyethylene glycol (a water-soluble

polymer) (see abstract; col 2, line 8 to col 5, line 40). This satisfies instant claims 11 and 17. The controlled release core comprises 50 mg tramadol hydrochloride (see col 6, lines 8-31), which satisfies instant claim 21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-12, 17, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6156342 ('342). The relevant portions of '342 are given above. Additionally, '342 teaches that cellulose acetate may be present in 39.3 to 40.3% (see col 4, lines 59-62), which anticipates Applicant's range of about 20% to about 90%. The plasticizer may be present in about 0% to about 30% (see col 5, lines 37-40) and polyethylene glycol may be present from approximately 0% to about 50% (see col 5, lines 21-23). '342 fails to teach about 5% to about 30% plasticizer. '342 further fails to teach about 10% to about 75% polyethylene glycol.

It would have been obvious to one of ordinary skill in the art to optimize the amounts of plasticizer and polyethylene glycol in the coating, through routine experimentation, to improve the efficacy of the formulation. In this way, one would find weight percent ranges given in instant claim 12. '342 provides sufficient guidance to this end, as about 5% to about 30% plasticizer in Applicant's claims overlaps with about 0% to about 30% taught by '342. Similarly, about 10% to about 75% polyethylene glycol overlaps with approximately 0% to about 50% taught by '342. "'[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" MPEP § 2144.05, II.

Claims 1, 4 and 11-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5601842 ('842) in view of US 6350471 ('471). '842 discloses that tramadol hydrochloride is an analgesic effective in treating severe and moderate pain (see col 1, line 14 to col 2, line 29). All drug formulations available on the market are immediate release forms which require administration 3 to 4 times per day in order to achieve good therapeutic effectiveness in relieving chronic pain. It would be a desirable relief to the patients if the frequency of administration could be reduced to once or twice daily (see col 1, lines 14-23). A controlled release formulation of the drug is therefore desirable (col 2, lines 34-56). '842 fails to disclose the modified release pharmaceutical composition of tramadol hydrochloride disclosed in the instant claims.

'471 discloses a controlled release composition that is desirably free of pore-formers and stabilizers and provides release of the active agent over 24 hours (see col 3, lines 4-21). The formulation comprises (i) a core comprising the active agent, polyvinyl alcohol (a binder), colloidal silicon dioxide (a glidant), and sodium stearyl fumarate (a lubricant); and (ii) a coating comprising ethylcellulose (a water-insoluble, water-permeable film-forming polymer), polyvinylpyrrolidone (a water soluble polymer), and dibutyl sebacate (a plasticizer). Ethylcellulose is present between 20 to 85% of the coating dry weight. Polyvinylpyrrolidone is present between 10 to 75% of the coating dry weight. Dibutyl sebacate is present between 5 to 30% of the coating dry weight. These ranges anticipate the ranges disclosed in instant claim 12. The composition, which may be in the form

of a tablet, comprises 0.1 to 1500 mg active agent per tablet (see col 3, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to incorporate tramadol hydrochloride as the active agent in the formulation of '471. In this way, a controlled release formulation of tramadol will be made that, relative to immediate release forms, reduces the frequency of administration to once or twice per day while still achieving therapeutic effectiveness in relieving chronic pain. The formulation would have the further benefits of being free of pore-formers and stabilizers. It would have been obvious optimize the dosage of tramadol hydrochloride to maximize the drug's efficacy while reducing unwanted side effects. In this way, one would find the value of 50 mg tramadol hydrochloride, through routine experimentation, as this value overlaps with the value of active agent taught by '471 of 0.1 to 1500 mg.

Regarding the release profiles recited in instant claims 1 and 4, '842 and '471 are silent on this property. However, a composition cannot be separated from its properties. Based on the substantially identical process using identical components, the Examiner has a reasonable basis to believe that the properties claimed in the present invention would be inherent in the formulation rendered obvious by '842 in view of '471. ""[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d

1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." MPEP § 2112, I.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric E Silverman/
Primary Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

January 15, 2010